Aventis Pasteur

15 '01 NOV

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

15 November 2001

Re: Docket No. 01D-0221
Guidance for Industry- Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components, Draft Guidance; 66 Fed Reg. P 42547-42548 (August 13, 2001)

Dear Sir/Madam:

Aventis Pasteur is pleased to provide the following comments on the above-referenced draft guidance for industry entitled "Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components." The guidance would revise the agency's existing guidance on biological product deviation reporting and assist responsible parties in fulfilling FDA's product deviation reporting requirements for marketed human biological products.

Aventis Pasteur strongly supports FDA's efforts in providing industry with guidance in fulfilling biological product deviation reporting requirements. We are directly affected by this guidance and offer the following comments for your consideration.

General Comments

- Throughout the referenced draft guidance document, 21 CFR 820 is referenced although this is not a guidance document for the Medical Device industry. All references to 21 CFR 820 should carry the same statement, "Biological device manufacturers are subject to Medical Device Reporting in accordance with 21 CFR 8XX."

- Many of the examples cited deal with blood/blood products although the referenced draft guidance document specifically excludes them in the title.

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- The Biological Products Deviation Report may be submitted electronically. What has been done to ensure a secure system? What would prevent anyone from submitting a Biological Products Deviation Report in our name?

Specific Comments

- Page 5. The draft guidance document states: "The decision to report should not be based on an investigation into whether the event affected the safety, purity or potency, but whether the event had the potential to affect the safety, purity, or potency of a product."

  Further, on Page 10, the draft guidance document states: *"If you discover a deviation or unexpected event after distribution of any affected product and the safety, purity, or potency of the product may have been affected at the time of distribution, you are required to report the event. You must report the event under 21 CFR 600.14 even if you determine through investigation, that the safety, purity, and potency of the product was not affected".* However, just before that statement on Page 10, an apparent contradiction occurs. The draft guidance document states: "If an event occurred, but could not affect the safety, purity or potency of a product, it must be recorded, evaluated and investigated in accordance with 21 CFR 211.192 and 211.198 for drug products and 21 CFR 820.90 and 820.100 for device products, but no biological product deviation report to FDA is required.

  There is no way to determine whether the deviation may effect, had the potential to effect, could effect, etc. without investigating. Once the investigation determines there was no effect, there should be no need to report. This creates an undue burden for reporting. Any "event" has the potential to effect the safety, purity or potency of a product. It is the investigation that determines whether the event did, in fact, effect the product.

- In the examples cited on Page 15, a power outage is considered a reportable event. If a power outage occurs, is thoroughly investigated and it is determined that the outage had no effect on the product, before the product is distributed, why should it be reported following distribution?

- In the examples cited on Page 15, "Environmental Monitoring does not meet established specifications." We presume this means if it is found after a lot has been distributed.

- The requirement to report any deviation or unexpected event discovered after distribution, even if the investigation showed there was no impact on the safety, purity or potency, seems inconsistent with the allowance to investigate product within our control and distribute after determination that the safety, purity & potency were not effected.

- The guidance document could be clearer on the impact of a material not meeting a particular specification. As the guidance reads, any material or component which does not meet its specification (presumably as filed) and not picked up before distribution requires reporting. It would be possible for a minor shift in the diameter of a vial to take it outside spec, but to have no effect whatsoever on the safety, purity & potency. In this case, manufacturers should be obliged only to investigate and document, but not to report.

- There seems to be a clear link, in this document's definition, between safety, purity & potency and cGMPs. While this may be the case, it is evidently not true to say that non-compliance with cGMPs gives a product that is not safe, pure or potent.

- Under IV F, it appears that we would be required to report product shipped at incorrect temperature or with lack of assurance that controlled temperatures were maintained during shipment when controlled storage is required (applies to distributed product). This would be in spite of knowing from accelerated stability studies that the product would not have been effected. This seems excessive if stability data is in place to make sound decisions to use or discard product.

- Complaints that generate internal deviation reports and investigation may also be reportable. The assumption being that if the deviation was discovered after distribution, it may have had impact on safety, purity or potency that we were unaware of at the time. This includes deviations for product or material specifications AND process parameters.

Aventis Pasteur appreciates the opportunity to comment on the referenced draft guidance document and we thank you for your consideration of our comments.

Sincerely,

Maureen D. Harmon, Ph. D.

for Ricky D. Smith
Acting Site Head,
Regulatory Affairs
and Authorized Official

RDS/MWH/kh

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